ABSTRACT OF THE DISCLOSURE

Methods for the identification, production and use of staphylokinase derivatives characterized by a reduced immunogenicity after administration in patients. The derivatives of the invention are obtained by preparing a DNA fragment comprising at least the part of the coding sequence of staphylokinase that provides for its biological activity; performing *in vitro* site-directed mutagenesis on the DNA fragment to replace one or more codons for wild-type amino acids by a codon for another amino acid; cloning the mutated DNA fragment in a suitable vector; transforming or transfecting a suitable host cell with the vector; culturing the host cell under conditions suitable for expressing the DNA fragment; and purifying the expressed staphylokinase derivative to homogeneity. Preferably the DNA fragment is a 453 bp *Eco*RI-*Hind*III fragment of the plasmid *pMEX602sakB*, (*pMEX.SakSTAR*), the *in vitro* site-directed mutagenesis is performed by spliced overlap extension polymerase chain reaction and the mutated DNA fragment is expressed in *E. coli* strain TG1 or WK6. The invention also relates to pharmaceutical compositions comprising at least one of the staphylokinase derivatives according to the invention together with a suitable excipient, for treatment of arterial thrombosis.